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THIRTY YEARS OF USSR VETERINARY PHARMACOLOGY

Prof I. Ye. Mozgov

Before the revolution there was, properly speaking, no veterinary pharmacology in Russia. This discipline was taught by medical pharmacologists, or more often by pharmacists or physiologists. Medical textbooks were used and the course did not differ in any respect from the regular medical course. This state of affairs changed after the October Revolution, because veterinary education was encouraged and a firm basis laid for the development of veterinary pharmacology.

Prof N. A. Soshestvenskiy (deceased) must be regarded as the founder of Russian veterinary pharmacology. The majority of USSR veterinary pharmacologists are pupils of Soshestvenskiy or of his pupils. He created the first Russian manuals of veterinary pharmacology and veterinary toxicology. The principal aim of his activity was to apply profound theoretical studies in such a way as to satisfy the demands of the national economy. He studied extensively the action of chlorine and of chlorine derivatives which were introduced into the practice of mass disinfection. His experimental data on the action of sulfur dioxide formed the basis for the treatment of mange with this substance. Soshestvenskiy's work on the pharmacodynamics of yperite, chloropicrin, and stimulants is of great scientific importance.

USSR veterinary pharmacology did not develop as a narrowly specialized science. It branches out into independent sciences such as phytotoxicology, toxicology of chemical warfare agents, and disinfection.

The achievements of USSR veterinary pharmacology during World War II were particularly striking. During this period, extensive investigation on nerve stimulants, sulfa drugs, chemotherapeutic agents, stimulants of wound healing, and anti-inflammatory agents was carried out.

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The production of drugs was developed on an extensive scale under the Soviet regime. In 1946, the quantity of drugs used in veterinary medicine was 36 times larger than in 1913. After the October Revolution, scientific work devoted to the development of new drugs and to the clarification of the composition of the most effective foreign drugs was sharply accelerated. During the past 30 years [1917 - 1947], the constitution of all drugs that were of interest was cleared up. In addition to that, many new substances were synthesized and introduced into production. Together with the synthesis of drugs and industrial production of synthetic pharmaceuticals, investigation of domestic sources of drugs of botanical origin was conducted. As a result of this work, the demand of the national economy for drugs was satisfied completely by the domestic pharmaceutical industry. Although this demand increased, importation of drugs from abroad became unnecessary.

Research in the Field of Pharmacodynamics

Pharmacological research has shown that a chemical substance may exert diverse effects. Simple substances like inorganic acids and alkalis may either stimulate or suppress individual functions of cells. Many alkaloids act similarly to enzymatic catalysts on specific functions of individual tissues. Ethyl alcohol acts not only as a narcotic, but also as a stimulant, and, furthermore, as an energy-supplying substance; the last two types of action are especially pronounced in herbivorous animals. Substances like camphor and caffeine, which stimulate the action of the central nervous system and many other functions of the organism, should be administered in doses that are just large enough to restore the weakened function. Administration of high therapeutic doses of these substances, as practiced before, harms the organism.

The pharmacodynamics of substances acting on the vegetative nervous system were studied very thoroughly from every angle. It was established that stimulation of the vegetative nervous system is connected with the production of specific substances, the so-called mediators (choline, acetyl choline, and sympathin) or suppression of enzymes which decompose these mediators. In view of the fact that synthetic choline or acetyl choline is too unstable, carbocholine [carbamyl choline chloride] has been introduced into veterinary practice and is widely used at present.

Much work has been done in studying the action of cardiovascular agents. The significance of the carotid sinus zone in connection with the action of this class of substances was demonstrated. The characteristics of the action of these substances in various pathological conditions were established, and the effect on the muscles and the heart was clarified.

The reflex mechanism involved in the action of a large number of expectorants and laxatives was investigated. The data obtained in this work permitted the application of this class of substances in veterinary practice.

The anti-inflammatory action of a very extensive group of substances has been subjected to thorough study. The following have been investigated: alterations which the reticuloendothelial system, the arterial blood vessels, and the veins undergo as a result of the action of drugs; the permeability of blood vessels; the barrier function of cells; phagocytosis; metabolism; and tonus of the vegetative nervous system. The effects which the conditions involved in these phenomena have on the process of inflammation were clarified. The mechanism of the anti-inflammatory action of derivatives of bismuth, zinc, lead, aluminum, silver, iodine, and mercury, as well as vitamins, fish liver oil, phenols, cresols, organic dyestuffs, astringents, adsorbents, and coating materials, has been investigated thoroughly.

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Among disinfectants, derivatives of chlorine, iodine, sulfur, and mercury, as well as oxidants, acids, alkalis, phenols, cresols, and organic dyestuffs, have been investigated with particular thoroughness.

Among drugs effective against mange, cresol preparations, sulfur preparations, and "K" soap have been investigated. In the field of antihelminthics, work has been done on carbon tetrachloride, male fern, oil of chenopodium, santonin, tartar emetic, thymol, hexachloroethane, tetrachloroethylene, phenothiazine, etc.

As far as chemotherapeutic agents are concerned, the following substances have been studied: trypan blue, flavacridine [acrivlavine?], rivanol, piroplasmin [acaprin; 6, 6' - ureylene-bis (1, 1' - dimethylquinolinium sulfate)], naganin [Bayer 205; germanin; Fourneau 309], sulfanthrol [sodium salt of sulfanilylanthranylic acid] and other sulfa drugs, antibiotics, etc.

Work on the investigation of the mechanism of the action of drugs was carried out by veterinary as well as medical pharmacologists. It was not possible to separate the activities of these two groups. Of the greatest importance was the work of veterinary pharmacologists in determining the action of drugs as related to the dosage, the species of animal, and particularly the pathological process. The following persons participated in the research in question: N. A. Soshestvenskiy, A. M. and L. M. Preobrazhenskiy, P. I. Popov, N. P. Govorov, A. I. Kuznetsov, S. G. Sidorova, G. D. Volkov, V. P. Petrov, P. Ye. Radkevich, N. Ye. Karneyev, G. S. Nazarov, I. A. Storozhev, V. N. Zolotov, P. D. Yevdokimov, P. G. Men'shikov, A. P. Lokk, D. K. Chevyakov, D. R. Dzhaferov, G. I. Gelavani, V. G. Loshchinskiy, M. V. Kazanova, Ye. V. Petrova Ye. I. Ayrepetyan, A. M. Priselkov, A. R. Yevgrafov, L. A. Fadeyev, N. N. Bogdanov, I. I. Magda, I. Ye. Mozgov. As a result of the described activity, many new, more effective drugs were introduced into veterinary clinical practice. Extensive experimental results, to be used in future work on the synthesis of drugs, were accumulated.

Domestic Drugs of Botanical Origin

Many botanical drugs were used for a long time in popular medicine, but were not subjected to scientific investigation. Only during the past 20-25 years did these drugs receive systematic scrutiny in the laboratory and clinic, with the result that many of them were introduced into therapeutic practice.

In the course of work done by veterinary pharmacologists, it was established that many drugs which were imported for scores of years, can be grown (and are already being grown) in the USSR. This applies to subtropical plants like sabur [Aloe ferox], cassia, etc. Other imported drugs are being replaced by domestic botanical drugs which are equally effective; thus, the use of vatochnik [Asclepias cornuti or A. syriaca] instead of strophanthus has been proposed.

As a result of the study of botanical drugs, chemists working in collaboration with pharmacologists were able to isolate the active principles of a large number of these drugs. Many of the substances representing these active principles were introduced into practice. The following substances were investigated exceptionally well: platyphyllin, omnopon [pantopon], papaverine, ephedrine, lobeline, cytisine (cytitone), ergotin, domestic camphor, oil of turpentine, ascorbic acid, and nicotinic acid. Work on drugs of botanical origin was carried out at the pharmacological laboratories of the Moscow Zoological-Veterinary Institute, the Omsk, Kazan', and Buryat-Mongol Veterinary Institutes, the All-Union Institute of Experimental Veterinary Medicine, etc.

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Introduction of New Chemotherapeutic Agents Into Veterinary Practice

The new substances being introduced into practice are more effective and more easily available than the old ones. For instance, ordinary flavacridine, which has a toxic effect on protoplasm, should be replaced by neutral flava-cridine, which does not irritate tissues. Other alternatives are proflavine, which is a simple and nonirritating substance, neutral sulfanthrol, or the non-irritating novoplasmin [methylsulfomethylate of N,N'-di-(4-dipropylaminophenyl)-urea]. The greatest achievements in this field are represented by the study of means of causal therapy as follows: streptocide, sulfidine [sulfapyridine], sulfanthrol novoplasmin, proflavine, piroplasmin, novarsenol [neocarsphenamine], myarsenol, sur'min [stibosan], and antibiotics. Work in this connection was done by I. I. Kazanskiy, P. I. Popov, A. I. Shmulevich, and I. Ye. Mozhgov.

Results achieved in the fight against blood parasites are visible evidence of the fact that means of causal therapy represent a powerful weapon in the hands of the physician. Still more significant is introduction of specific bactericidal agents. The harmful view, held since Ehrlich's time, to the effect that it is impossible to find substances which would have a specific action against definite bacteria has been disproved. USSR epizootologists, who formerly placed their reliance entirely on biological preparations, have been induced to investigate the application of synthetic chemotherapeutic agents. The introduction of sulfa drugs into practice must be regarded as a milestone which marked the beginning of the search for further specific therapeutic agents. This development led to consideration of the possibilities offered by antibiotics.

There is not a single branch of veterinary science in which the achievements of USSR pharmacology have not been utilized on the widest scale. Several additional examples of this will be given below.

Remedies for Mange

Considerable attention has been paid to the investigation of remedies for mange, including sulfur dioxide, creolins, lysols, arsenicals, etc. Work in connection with these remedies was done at the Moscow Zoological-Veterinary Institute, the State Dermatological Institute, the Saratov Zoological-Veterinary Institute, the All-Union Institute of Experimental Veterinary Medicine, etc. As a result of the investigations in question, several new remedies were devised and new methods of therapy advanced. The gas-chamber method of treating horses with sulfur dioxide has been widely introduced. This method has been put into practice and has yielded good results. Several formulas of creolins and lysols have been proposed for the treatment of mange of sheep. These formulas are being successfully applied in sheep dips and liniments. New are the hyposulfite method of Dem'yanovich and the dry hyposulfite-bisulfate method.

Disinfectants

The action of chlorine, chlorine water, calcium hypochlorite, chloramines, formaldehyde, acids, alkalis, ash, salts of heavy metals, etc., has been thoroughly investigated. Disinfection has become an indispensable part of veterinary sanitation and antiepidemic measures. The science of disinfection has become a separate scientific discipline.

Stimulants

As far as general stimulants are concerned, corazole [cardiazole; metrazole] and coriamine [coramine?] have been proposed. These substances exert a stimulating action on the central nervous system (like strychnine), improve the action of the heart (like caffeine), raise the blood pressure (like camphor), and also lower the sensitivity of the heart muscle to various toxins and poison.

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The effect of camphor on the healthy and diseased organism has been investigated in great detail. The action of hexeton /homocamfin/, a camphor isomer which has some advantages in comparison with ordinary camphor, has also been subjected to a thorough study. This work was done by V. V. Savich, N. I. Govorov, A. I. Kuznetsov, V. N. Zolotov, and D. R. Dzhabarov. The pharmacodynamics of turpentine, which is widely used in veterinary medicine as a specific and nonspecific stimulant, have been clarified.

In regard to cardiac glucosides, attempts to replace the scarce strophanthin have already been mentioned. The dosages and indications for the application of gitalin, diginorm, and adonilen have been worked out more precisely.

Vegetotropic Substances

Besides study of the action of atropine, pilocarpine, arecoline, physostigmine, and adrenaline, much attention has been devoted to the pharmacodynamics of carbacholine, platyphyllin, and ephedrine, and to the introduction of these drugs into practice (P. I. Popov, Ye. V. Petrova, A. I. Kuznetsov, I. Ye. Mezgov). Generally speaking, carbacholine has already replaced other vagotropic substances (arecoline, pilocarpine) which had been used widely in pathological conditions of the gastrointestinal tract. Platyphyllin has many advantages in comparison with atropine, because its action is milder and is accompanied by fewer side effects.

Narcotics

The scientific theory underlying the application of narcotics has undergone a thorough revision. As a result, chloral hydrate and alcohol have been proposed and approved as basic substances to be used in producing narcosis in animals. Two new substances, narcolan /avertin/ and hexenal, have been introduced.

Pharmacology of the Digestive Tract

The greatest number of experimental investigations has been devoted to the pharmacology of the digestive tract. The mechanism of the action of new laxatives (carbacholine, domestic senna, sabur /aloe/, istizin /1,8-dihydroxy-anthraquinone/, calomel, and popular remedies) has been investigated and the optimum conditions for their application determined. A great number of disinfectants and anti-inflammatory agents has been studied and introduced into practice. Among them the following may be mentioned: streptocides, sulfazole /2-sulfanilylamino-4-methyl thiazole/, disulfan /4-sulfanilyl-anilide of sulfanilic acid/, sulfanthrol, calomel, osarsol /acetarsone/, alcohol, analgin $[C_{13}H_{16}O_4N_3SNa + H_2O]$, bismuth derivatives, cresols, yatren /chiniofon/, tannin and its complex salts, combinations of adsorbents with disinfectants and anti-inflammatory agents. The following substances, after having been investigated from this point of view, are now being used as analgesics in diseases of the digestive tract: alcohol, analgin, platyphyllin, omnopon. The work in question was done by N. A. Soshestvenskiy, A. R. Efgrafov, N. I. Govorov, N. I. Shokhor, G. D. Volkov, D. K. Nechinenny, and I. Ye. Mazgov.

Oxytocics and Gonadotropic Substances

Pituitrin, prolan, and sinoestrol /diethylstilboestrol/ have been submitted to investigation.

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Substances Stimulating Wound Healing and Anti-Inflammatory Agents

During recent years, a considerable amount of work has been done on substances which stimulate healing and have an anti-inflammatory action. The nature of tissue alterations taking place under the action of drugs at various stages of the inflammation process has been clarified. Methods of applying local anesthetics have been developed. A great number of new therapeutic agents of this class has been introduced into practice. Many prescriptions that involve combined action of drugs have been developed.

The substances studied to the greatest extent include novocaine, dicaine, thiocaine [$C_{13}H_{20}ON_2S \cdot HCl$], sovaine [percaine] hydrogen peroxide, perhydrit, metal peroxides, "chlorazide," mercury derivatives, ammargen, silver nitrate, compounds of zinc, bismuth, aluminum, lead, and iron, new cresol preparations, quinosol, entozon [cf. Chemical Abstracts, 43, 4382d, 1949], pyoktanin, flavacridine, proflavine, rivanol, brilliant green, streptocides, reversible emulsion, sulfidine, sulfazole, disulfan, gramicidin, penicillin, fish liver oil, and ascorbic acid.

USSR veterinary pharmacologists have correctly understood the task of pharmacology, which comprises a thorough study of the most effective and easily accessible drugs and their introduction into veterinary practice.

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